required to deal with the altered brain function and the concomitant behavioral and social functioning components of the illness.

Understanding addiction as a brain disease explains in part why historic policy strategies focusing solely on the social or criminal justice aspects of drug use and addiction have been unsuccessful. They are missing at least half of the issue. If the brain is the core of the problem, attending to the brain needs to be a core part of the solution.

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Interpreting Dutch Cannabis Policy: Reasoning by Analogy in the Legalization Debate

Robert MacCoun and Peter Reuter

The Dutch depenalization and subsequent de facto legalization of cannabis since 1976 is used here to highlight the strengths and limitations of reasoning by analogy as a guide for projecting the effects of relaxing drug prohibitions. While the Dutch case and other analogies have flaws, they appear to converge in suggesting that reductions in criminal penalties have limited effects on drug use—at least for marijuana—but that commercial access is associated with growth in the drug-using population.

Illicit drugs continue to be a major source of health and social problems in the United States, accounting for 35% of new cases of acquired immunodeficiency syndrome (*1*) and about $50 billion in criminal income (*2*). Large declines in prevalence have occurred since the mid-1980s—10.7% of the household population reported use of an illicit drug in the previous year in 1995, compared with 16.3% in 1985 (*3*)—but most measures of adverse consequences have risen or stabilized. Heroin-related deaths recorded by Medical Examiners in 25 metropolitan areas rose from 1300 in 1985 to 3500 in 1994 (*4*).

U.S. drug policy is heavily committed to a punishment-based approach. This is reflected in budgets; two-thirds of the federal government's $16 billion expenditures go to supply-reduction programs (*5*), whereas state and local governments, estimated to spend $18 billion, probably devote 75 to 80% to policing, prosecution, and corrections (*6*). About 400,000 individuals are currently incarcerated in jails or prisons for violation of drug laws (*7*). Moreover, treatment and prevention programs are frequently required to show that they are cost-effective, a standard never imposed on drug enforcement (*8*). Penalties have increased whenever a drug becomes more prominent, as for example in the new federal methamphetamine statute (*9*). The probability of a cocaine or heroin seller being incarcerated has risen sharply since about 1985 (*10*), but that has led neither to increased price (*11*) nor reduced availability (*12*).

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The Legalization Debate

Given the persistence of a major drug problem despite expensive, intrusive, and harsh policies, it is not surprising that there has been a continuing debate in the United States about the desirability of major changes in that policy, indeed a shift in the basic regime (*13*). Some press for depenalization (often misleadingly termed decriminalization), the removal of criminal penalties for the simple possession of drugs; a smaller number press for the more radical step of legalizing the distribution of any psychoactive substance, subject to civil regulation (*14*). Few commentators distinguish among drugs in debating these recommendations.

The debate about legalization invokes conflicts in values, with legalizers emphasizing the threat that prohibition poses to civil liberties (*15*) and opponents the hedonism and self-centeredness of drug taking (*16*). However, the debate also exposes gross discrepancies in predictions of the effects of legalization on levels of drug use. Legalizers point to the failure of increasing enforcement to raise prices or decrease availability as evidence that legalization would not much increase use or dependence (*17*), while their opponents emphasize the importance of symbolic and real barriers to initiation associated with prohibition to suggest that legalization would produce massive increases in these rates (*18*).

There are three general strategies for projecting the likely consequences of a change in the legal regime for drugs. First, one can draw upon existing theory and research. But for a variety of reasons (*19*), research on variations in drug law enforcement within a prohibition regime cannot be extrapolated outside that regime, and existing theories provide an uncertain guide to the net consequences of such interventions. Legal change is far more fundamental than

simply elimination of the risk of arrest and punishment. It affects the price, availability, and quality of drugs; marketing and advertising practices; attitudes and norms; social stigmas; and other factors in complex and interrelated ways (*19*). As a second strategy, one can conduct a demonstration experiment, or a quasi-experimental program evaluation. Serious political, legal, ethical, and logistical obstacles make the chances of such demonstrations rather remote. Switzerland has just concluded partially controlled clinical trials of heroin maintenance, in which addicts receive either methadone or heroin from treatment providers (*20*). Even though this intervention falls well short of legal commercial access to heroin, it is the object of intense and skeptical scrutiny from other nations and from international regulatory bodies.

Thus, the legalization debate has relied heavily on a third strategy: projecting the effects of depenalizing or legalizing drugs in the contemporary United States on the basis of analogies to experiences of other places, historical periods, substances, or behaviors. For example, policy elites and social scientists frequently draw inferences from the U.S. experience with legal cocaine in the 1890s, Alcohol Prohibition in 1919 and Repeal in 1933, marijuana depenalization in many states in the 1970s, the British experiences with legal prescription of heroin to addicts until 1967, and contemporary regulation of tobacco (*21*). In this article, we examine the Dutch cannabis regime, a prominent analogy in the debate.

"De Facto" Legalization in the Netherlands

The Dutch cannabis experience provides an excellent illustration of both the strengths and limitations of reasoning by analogy (*22*). It is not uncommon in the United States to hear assertions that "the Dutch have legalized drugs," resulting in a total disaster or a remarkable breakthrough, depending on the speaker's hawkish or dovish drug-policy leanings. But a closer examination suggests that the actual Dutch policies are considerably more nuanced and the results more ambiguous than is generally understood, and that drawing lessons for the United States is extremely difficult.

Policy. It is true that Dutch drug policy is more explicitly tolerant than that of any other Western industrial nation, although few Americans realize that drugs are depenalized in both Italy and Spain. The Dutch impose no penalties for the possession of small amounts of cannabis, allow a number of coffee shops to openly sell that drug, and were among the first to pioneer needle exchange and other policies to reduce the harms that drug users pose to themselves and others (*23*). But the complexity of the Dutch regime points to the danger of "Policy Platonism"—treating policy regimes as ideal types. This unusual cannabis regime falls partway between the depenalization of cannabis possession and the complete legalization of cannabis sales. It is part of a long Dutch tradition of "gedoogbeleid"—the formal, systematic application of discretion—and one element in a more comprehensive philosophy known as harm reduction or harm minimization.

In compliance with their international treaty obligations, Dutch law states unequivocally that cannabis is illegal. Yet in 1976 the Dutch adopted a formal written policy of nonenforcement for violations involving possession or sale of up to 30 g of cannabis—a sizable quantity, since few users consume more than 10 g a month (*24*). In late 1995, this threshold was lowered to 5 g in response to domestic and international pressures (*25*). Moreover, a formal written policy regulates the technically illicit sale of those small amounts in open commercial establishments; as of late 1995, a 500-g limit on trade stocks was established. Enforcement against those supplying larger amounts is aggressive; in 1995 the Dutch government seized 332 metric tons of can-

Table 1. Prevalence of cannabis use in the Netherlands, USA, Denmark, and Germany.

Age group	Year	Type of prevalence	Dutch location	Prevalence (%)	Contrast location	Prevalence (%)	Difference (%)
			Netherlands versus USA†*				
12 to 17	1992	Lifetime	Netherlands	12.6	USA	10.6	2.0
Approx. 18	1992	Lifetime	Netherlands	34.5	USA	32.6	1.9
Approx. 18	1996	Lifetime	Netherlands	44.0	USA	44.9	−0.9
						Mean difference:	1.0
			Tilburg‡ (population 165,000) versus USA†				
12 and older	1995	Past month	Tilburg	2.4	USA	4.7	−2.3
12 and older	1995	Past year	Tilburg	4.0	USA	8.4	−4.4
						Mean difference:	−3.4
			Utrecht‡ (population 235,000) versus USA†				
12 and older	1995	Past month	Utrecht	4.3	USA	4.7	−0.4
12 and older	1995	Past year	Utrecht	8.2	USA	8.4	−0.2
						Mean difference:	−0.3
			Amsterdam§ (population 7000,000) versus USA†				
12 and older	1994	Past month	Amsterdam	6.7	USA	4.7	2.0
12 and older	1994	Past year	Amsterdam	10.5	USA	8.5	2.0
35 and older	1994	Past month	Amsterdam	3.5	USA	2.3	1.2
						Mean difference:	1.7
			Netherlands versus Denmark				
Approx. 18	1990	Lifetime	Netherlands‖	28.0	Copehagen¶	52	−24.0
20 to 24	1994	Past year	Amsterdam§	25.0	Denmark#	16.0	9.0
25 to 29	1994	Past year	Amsterdam§	18.2	Denmark#	7.0	11.2
						Mean difference:	−1.3
			Amsterdam§ versus West Germany				
12 to 29	1990	Lifetime	Amsterdam	33.0	W. Germany¶	16.0	17.0
25 to 29	1994	Past year	Amsterdam	18.2	W. Germany#	5.6	12.6
						Mean difference:	14.8

*Data are from (*31*). †Data are from the National Household Survey on Drug Abuse, various years. ‡Data are from (*29*). §Data are from (*32*). ‖1990 figure interpolated from 1988 and 1992 estimates in. (*31*). ¶Data are from (*51*). #Data are from (*52*).

nabis, about 44% of the total for the European Union as a whole (*23*).

Between 1976 and 1986, a set of guidelines emerged stipulating that coffee shop owners could avoid prosecution by complying with five rules: (i) no advertising; (ii) no hard drug sales on the premises; (iii) no sales to minors; (iv) no sales transactions exceeding the quantity threshold; and (v) no public disturbances (*23*, *26*, *27*). In 1980, Ministry of Justice guidelines decentralized implementation, providing greater local discretion. As a result, enforcement became more lenient in Dutch cities, and somewhat stricter in smaller towns (*27*). The effect is illustrated graphically in Dutch geographer A. C. M. Jansen's maps plotting cannabis coffee shop locations in Amsterdam (*27*). He depicts 9 locations in 1980, 71 in 1985, and 102 in 1988, noting that "the first coffee shops were usually situated in unattractive buildings in backstreets . . ." (*27*, p. 69), but that over time the shops have spread to more prominent and accessible locations in the central city; they also began to promote the drug more openly. The Dutch argue that this system of quasi-legal commercial availability not only avoids excessive punishment of casual users, but also weakens the linkage between soft- and hard-drug markets.

Outcomes. The cumulative effect of formal, quasi-formal, and informal policies is to make cannabis readily available at minimal legal risk to interested Dutch adults. Somewhere between 1200 and 1500 coffee shops (about 1 per 10,000 inhabitants) sell cannabis products in the Netherlands (*23*). Most offer an international variety of marijuana and hashish strains of varying potency levels. Gram prices are 5 to 25 guilders ($2.50 to $12.50) (*28*) compared with U.S. figures of $1.50 to $15.00. The continued high price of marijuana in the Netherlands probably reflects the aggressive enforcement against large-scale growers and distributors. The clientele appear to be predominantly young adults from a wide range of social backgrounds, including tourists—a point of contention in Holland's relations with France, Germany, and Belgium (*26*).

There are three key policy questions. First, are levels of cannabis use higher in the Netherlands than in other Western nations? Second, did levels of cannabis use in the Netherlands increase after the 1976 depenalization and subsequent de facto legalization? Third, has the policy change weakened the statistical association between marijuana and the use of other drugs? Below we examine the available cross-sectional and longitudinal data on cannabis use in the Netherlands, the United States, and several nations in Western Europe. No study has assessed cannabis use in the Netherlands and other nations with the same survey design and back-translated survey instruments. As a result, we are forced to compare surveys that vary with respect to question wording, sampling design, and so forth. The available surveys provide much better coverage of youth than of adult use. Although coffee shop regulations forbid sales to minors, adult availability is likely to facilitate secondary transactions involving minors, especially during the 1976 to 1995 period, before the 30-g limit was reduced to 5 g.

Prevalence of Cannabis Use in the Netherlands, USA, Denmark, and Germany

Are levels of cannabis use higher in the Netherlands than in other Western nations? At the very least, meaningful cross-sectional comparisons of drug use should be matched for survey year, measure of prevalence (lifetime use, past year use, or past month use), and age groups covered in the estimate. We have identified 15 comparisons that meet these criteria (Table 1). Ten involve Dutch-USA contrasts, three compare Dutch and Danish figures, and two compare Amsterdam with West Germany. All 15 occur in the 1990s, during the period we have characterized as de facto legalization, not just depenalization. Three contrasts compare national estimates from the Netherlands and the United States, with an average Dutch-U.S. difference of 1%, well within the sampling error of the surveys. The others involve U.S. national data and a Dutch city. Three contrasts pair the United States with an estimate from Amsterdam—a large urban setting with a highly visible drug culture. American surveys indicate little difference on average between large metropolitan samples and the United States as a whole (*3*), but the estimates in Table 1 suggest that smaller Dutch communities (Tilburg and Utrecht) have lower rates than Amsterdam. U.S. rates are lower than that of Amsterdam, similar to that of Utrecht, and higher than that of Tilburg (*29*).

The five contrasts between the Netherlands and her neighbors suffer from the same weakness: comparison of rates for an entire nation as a whole to those in the largest city of another nation. In 1990, 18-year-olds in the city of Copenhagen had considerably higher rates of cannabis use than their counterparts throughout the Netherlands. On the other hand, two contrasts suggest higher rates in Amsterdam than in Denmark as a whole. The final two contrasts indicate considerably lower rates of cannabis use in West Germany than in Amsterdam. Additional evidence, presented below, suggests that in recent years the Netherlands has had higher rates than Oslo, Norway. We conclude that Dutch rates now are comparable to that of the United States but somewhat higher than those of its neighbors.

Lifetime Prevalence of Cannabis in the Netherlands, USA, and Oslo, 1970 to 1996

Did levels of cannabis use in the Netherlands increase after the 1976 depenalization and subsequent de facto legalization? Figure 1 plots estimates from 1970 to 1996 of the

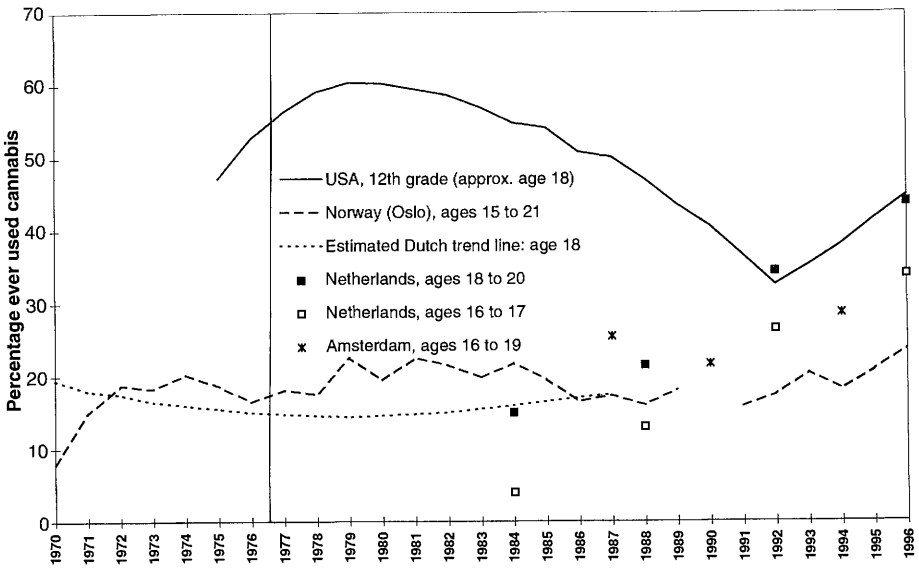

Fig. 1. Lifetime prevalence of cannabis in the Netherlands, United States, and Oslo, 1970 to 1996.

percentage of the Dutch population in various age groups who have ever used cannabis (30).

Since the mid-1980s, there have been two periodic surveys of drug use in the Netherlands: (i) the Timbos Institute national school-based survey covering the years 1984, 1988, 1992, and 1996 (31); and (ii) the University of Amsterdam's general population survey in Amsterdam, covering the years 1987, 1990, and 1994 (32, 33). In the period 1970 to 1983, the Netherlands lacked repeated, standardized drug surveys, so the existing data are piecemeal across time, geography, and question-wording. Two Dutch-language publications (34, 35) systematically review earlier surveys. Driessen and colleagues (35) conducted a multivariate analysis of data from 20 earlier surveys, statistically controlling for differences in age ranges, region, and survey characteristics. In Fig. 1, we plot their estimated trend line for lifetime cannabis use among 18-year-olds, 1970 to 1986. The trend line reasonably characterizes the available data, but we caution that these estimates do not form coherent time series like the Timbos and University of Amsterdam data.

These early survey estimates are our only window into the effects of the 1976 policy change on cannabis use. The trend line implies that among Dutch adolescents, cannabis use was actually declining somewhat in the years before the 1976 change, and that the change had little if any effect on levels of use during the first 7 years of the new regime (36). Unfortunately, we lack data on the stringency of enforcement in the years immediately before the change in law (37), although the trend lines are fairly smooth and declining for at least 6 years before 1976.

In the 1984 to 1996 period, which we characterize as a progression from depenalization to de facto legalization, these surveys reveal that the lifetime prevalence of cannabis in Holland has increased consistently and sharply. For the age group 18 to 20, the increase is from 15% in 1984 to 44% in 1996; past month prevalence for the same group rose from 8.5 to 18.5% (31). Is this an effect of the emergence of de facto legalization?

Two comparison series offer insight: The U.S. Monitoring the Future annual survey of high-school seniors (12), and an annual survey of Oslo youth, ages 15 to 21 (38). The United States and Norway both strictly forbid cannabis sales and possession, and aggressively enforce that ban. Because the Oslo survey has a broader age range, these estimates are more meaningful for comparing trends over time than absolute differences in prevalence in any given year.

The two comparison series behave very differently from the Dutch series, and from each other until 1992. The U.S. rates increase until 1979 and then fall steadily and substantially till 1992, whereas the Oslo figures increase sharply only until 1972 and then fluctuate around a flat trend until 1992. Interestingly, during 1992 to 1996, all three nations have seen similar large increases. This weakens the hypothesis that the Dutch increases from 1992 to 1996 are attributable to Dutch policies per se, although we acknowledge that the parallel nature of the increases might be coincidental. But survey data do indicate that a variety of individual and social risk factors influence marijuana use; policy variations may play a fairly minor role (39, 40).

The increases in Dutch prevalence from 1984 to 1992 provide the strongest evidence that the Dutch regime might have increased cannabis use among youth. Why would the removal of criminal penalties for possession and small-scale sales require 8 years to have an effect? We hypothesize that this is the consequence of the gradual progression from a passive depenalization regime to the broader de facto legalization that allowed for greater access and increasing levels of promotion, at least until 1995, when the policy was revised.

Table 2. Other case studies in the relaxation of drug laws.

Analogy	Drug	Drug availability	User Sanctions
Marijuana depenalization, 13 states, 1970s	Cannabis	Remained illegal	None or minor for small quantities
Italian and Spanish depenalization, mid-1970s to present	All street drugs	Remained illegal	None or minor for small quantities
British heroin prescription, 1925 to 1967	Heroin, other opiates	By physician's prescription	None if under prescription
Repeal of Prohibition, 1933	Alcohol	Commercially available	Little change
Legal cocaine, 1885–1914	Cocaine	Available in tonics and by prescription	None

Other Effects

Has the policy change influenced the statistical association between marijuana and the use of other drugs? An association between soft and hard drug use is necessary but not sufficient to establish a causal "gateway" mechanism (41). Although American hawks argue that more lenient cannabis policies might lead to greater levels of hard drug use, a central rationale for the 1976 Dutch legal change was the notion that separating the soft and hard drug markets might actually weaken any gateway effect (23). In Amsterdam, as in the United States, almost all hard drug users have used cannabis, but the vast majority of cannabis users have not used hard drugs. Only 22% of those aged 12 and over who have ever used cannabis have also used cocaine (42). This compares to a figure of 33% for the United States (43). Thus, although the Dutch have failed to eliminate the statistical association between cannabis and hard drug use—we estimate that the probability of cocaine use among those in Amsterdam who have never used cannabis is essentially zero (44)—it is possible that they have weakened it. Also, only 6% of cannabis users had used cocaine more than 25 times; only 2% were current (past month) users.

It is difficult to assess the effects of Dutch policies on cannabis-related harms for the simple reason that such harms generally go unmeasured everywhere. They go unmeasured in part because the average harm per user is so modest, and in part because those harms that do result from marijuana use are less tangible and less dramatic than the harms of crack or heroin.

Interpreting the Dutch Experience and Other Analogies

There is no evidence that the depenalization component of the 1976 policy, per se, increased levels of cannabis use. On the other hand, the later growth in commercial access to cannabis, after de facto legalization, was accompanied by steep increases in use, even among youth. In interpreting that association, three points deserve emphasis. First, the association may not be causal; we have already seen that recent increases occurred in the United States and Oslo despite very different policies. Second, throughout most of the first two decades of the 1976 policy, Dutch use levels have remained at or below those in the United States. And third, it remains to be seen whether prevalence levels will drop again in response to the reduction to a 5-g limit, and to recent government efforts to close down coffee

shops and more aggressively enforce the regulations.

What inferences can be drawn from the Dutch cannabis experience with respect to the U.S. legalization debate? There are three dimensions of generalization. First, would other modes of relaxing drug laws have the same effect as the peculiar Dutch blend of de jure prohibition and de facto legalization? Under true legalization, we would expect to see much steeper price declines, possibly leading to steeper increases in use. Second, would the consequences of relaxing cannabis laws generalize to policies for other drugs? Cannabis is generally considered much less addictive, criminogenic, and health-threatening than cocaine or heroin (*45*). And third, how well do experiences in the Netherlands generalize to the United States? It is possible that Dutch society differs from American society in ways that might influence cannabis consumption.

Other Case Studies in the Relaxation of Drug Laws

In recent work (*46*) we have been examining a diverse set of cases involving a variety of relaxations of drug laws in different times and places, and covering different substances (Table 2). Each poses inferential problems at least as thorny as those raised in this article. The principle of triangulation, however, suggests that flawed sources of data are more informative when their lessons converge rather than diverge, provided that the flaws are heterogeneous rather than homogeneous (*47*). Thus, analogies might be more helpful in the aggregate than individually. Across the cases, we do see some convergence with respect to depenalization effects. Marijuana depenalization in a dozen U.S. states in the 1970s (*40*) and depenalization of all drug use in Italy and Spain (*48*) seem to have a similarly modest effect to that of depenalization of cannabis in the Netherlands during 1976 to 1983. The additional evidence for our second conclusion, namely, that commercialization increases prevalence, is quite slight but also consistent. Repeal of alcohol Prohibition was not accompanied by a large increase in alcohol consumption for some years (*49*), but did rise sharply 15 years later when, inter alia, the regime of tight controls implemented at Repeal became less stringent and commercial promotion of liquor became more aggressive.

It is of course much easier to document the limitations of these analogies than to offer citizens and policy-makers positive guidance as to the likely effects of any major changes in drug policy. Moreover, a sound analysis of policy change needs to consider other complications not discussed here, including potential trade-offs between harm reduction and use reduction, the harms of drug use and of drug control, and potential shifts in the distributions of those harms across social groups (*50*). Some might argue that setting such high methodological standards biases the debate in favor of the status quo—an aggressive, intrusive, and expensive "war on drugs" with limited evidence of success and many detractors. But the ambiguity that clouds projections of legal change also argues against zealous, sweeping claims on the other side of the debate. For if we don't know what legalization would bring, we also know remarkably little about whether it is possible to achieve whatever consumption-reducing benefits our current version of drug prohibition provides, but in ways that mitigate its steep economic, social, and health costs.

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Drug Abuse: Hedonic Homeostatic Dysregulation

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Understanding the neurobiological mechanisms of addiction requires an integration of basic neuroscience with social psychology, experimental psychology, and psychiatry. Addiction is presented as a cycle of spiralling dysregulation of brain reward systems that progressively increases, resulting in compulsive drug use and a loss of control over drug-taking. Sensitization and counteradaptation are hypothesized to contribute to this hedonic homeostatic dysregulation, and the neurobiological mechanisms involved, such as the mesolimbic dopamine system, opioid peptidergic systems, and brain and hormonal stress systems, are beginning to be characterized. This framework provides a realistic approach to identifying the neurobiological factors that produce vulnerability to addiction and to relapse in individuals with a history of addiction.

Most definitions of drug addiction or substance dependence include (i) descriptions of "overwhelming involvement with the use of a drug (compulsive use)" (*1*) and (ii) a number of symptoms or criteria that reflect a loss of control over drug intake and a narrowing of the number of different behavioral responses toward drug-seeking (*2*). Drug addiction can be equated with substance dependence as defined by the American Psychiatric Association (*3*). However, it is important to distinguish between what is termed substance use, substance abuse, and substance dependence (addiction) (*4*).

In humans, most drug users do not become drug abusers or drug-dependent (*4*). Similarly, stable drug intake can be observed in animals without pronounced signs of dependence, even with intravenous drug administration under limited-access situations. Many factors such as availability (route of administration), genetics, history of drug use, stress, and life events contribute to the transition from drug use to drug addiction. The current challenge is to discover what neurobiological elements convey the individual differences in vulnerability to this transition to drug addiction.

In this article we will draw from recent formulations in behavioral neuroscience and other disciplines to construct a framework to view addiction as a continuous process of hedonic homeostatic dysregulation. Multiple sources of reinforcement are identified in the spiralling cycle of addiction, and the symptoms of this hedonic dysregulation form the well-known criteria for substance dependence or addiction (*2*, *3*). Critical neurotransmitters, hormones, and neurobiological sites have been identified that may mediate the hedonic dysregulation and may provide the substrates that convey both vulnerability to, and protection against, drug addiction (*5*) (Fig. 1).

Spiralling Distress and the Addiction Cycle

Important elements that may be involved in the failure to self-regulate drug use, as well as other behaviors such as compulsive gambling and binge eating, have derived from social psychology (*6*). It is of interest to conceptualize how these regulation failures ultimately lead to addiction in the case of drug use or an addiction-like pattern with nondrug behaviors. Lapse-activated causal patterns, that is, patterns of behavior that contribute to the transition from an initial lapse in self-regulation to a large-scale breakdown in self-regulation, can lead to spiralling distress (*6*). Spiralling distress describes how, in some cases, the first self-regulation failure can lead to emotional distress, which sets up a cycle of repeated failures to self-regulate, and where each violation brings additional negative affect (*6*). For example, a failure of strength may lead to initial drug use or relapse, and other self-regulation failures can be recruited to prevent an exit from the addiction cycle. Here, spiralling distress will be used to describe the progressive dysregulation of the brain reward system within the context of repeated addiction cycles (Fig. 1A).

Psychiatry and experimental psychology, in effect, address the same addiction cycle (Fig. 1B), and neurobiology has begun to identify the neurobiological elements that contribute to the break with hedonic homeostasis, known as addiction. Although animal models provide a critical part of the study of the neurobiology of addiction, no animal models incorporate all the elements of addiction. Alternatively, animal models can be established and validated for different symptoms or constructs associated with addiction (*7*). There is much evidence for valid animal models of many of the criteria in the fourth edition of *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) (*3*) and the sources of reinforcement associated with addiction (*7*).

Neurobiology of Drug Reinforcement

The focus for the neurobiological mechanism for the positive-reinforcing effects of drugs of abuse has been the mesocorticolimbic dopamine system and its connections in the basal forebrain (*8*, *9*). For cocaine, amphetamine, and nicotine, the facilitation of dopamine neurotransmission in the mesocorticolimbic dopamine system appears to be critical for the acute reinforcing actions of these drugs [for re-

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